



A434.ST25
SEQUENCE LISTING

43

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Ortwine, Daniel F
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Roark, William H

<120> Matrix Metalloproteinase Inhibitors

<130> A0000434-01-CFP Reg US App

<140> 10/075,069

<141> 2002-02-13

<150> 60/268,821

<151> 2001-02-14

<160> 1

<170> PatentIn version 3.1

<210> 1

<211> 471

<212> PRT

<213> Homo sapiens

<400> 1

Met His Pro Gly Val Leu Ala Ala Phe Leu Phe Leu Ser Trp Thr His
1 5 10 15

Cys Arg Ala Leu Pro Leu Pro Ser Gly Gly Asp Glu Asp Asp Leu Ser
20 25 30

Glu Glu Asp Leu Gln Phe Ala Glu Arg Tyr Leu Arg Ser Tyr Tyr His
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40

45

Pro Thr Asn Leu Ala Gly Ile Leu Lys Glu Asn Ala Ala Ser Ser Met
 50 55 60

Thr Glu Arg Leu Arg Glu Met Gln Ser Phe Phe Gly Leu Glu Val Thr
 65 70 75 80

Gly Lys Leu Asp Asp Asn Thr Leu Asp Val Met Lys Lys Pro Arg Cys
 85 90 95

Gly Val Pro Asp Val Gly Glu Tyr Asn Val Phe Pro Arg Thr Leu Lys
 100 105 110

Trp Ser Lys Met Asn Leu Thr Tyr Arg Ile Val Asn Tyr Thr Pro Asp
 115 120 125

Met Thr His Ser Glu Val Glu Lys Ala Phe Lys Lys Ala Phe Lys Val
 130 135 140

Trp Ser Asp Val Thr Pro Leu Asn Phe Thr Arg Leu His Asp Gly Ile
 145 150 155 160

Ala Asp Ile Met Ile Ser Phe Gly Ile Lys Glu His Gly Asp Phe Tyr
 165 170 175

Pro Phe Asp Gly Pro Ser Gly Leu Leu Ala His Ala Phe Pro Pro Gly
 180 185 190

Pro Asn Tyr Gly Gly Asp Ala His Phe Asp Asp Asp Glu Thr Trp Thr
 195 200 205

Ser Ser Ser Lys Gly Tyr Asn Leu Phe Leu Val Ala Ala His Glu Phe
 210 215 220

Gly His Ser Leu Gly Leu Asp His Ser Lys Asp Pro Gly Ala Leu Met
 225 230 235 240

Phe Pro Ile Tyr Thr Tyr Thr Gly Lys Ser His Phe Met Leu Pro Asp
 245 250 255

Asp Asp Val Gln Gly Ile Gln Ser Leu Tyr Gly Pro Gly Asp Glu Asp
 260 265 270

Pro Asn Pro Lys His Pro Lys Thr Pro Asp Lys Cys Asp Pro Ser Leu
 275 280 285

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Ser Leu Asp Ala Ile Thr Ser Leu Arg Gly Glu Thr Met Ile Phe Lys
290 295 300

Asp Arg Phe Phe Trp Arg Leu His Pro Gln Gln Val Asp Ala Glu Leu
305 310 315 320

Phe Leu Thr Lys Ser Phe Trp Pro Glu Leu Pro Asn Arg Ile Asp Ala
325 330 335

Ala Tyr Glu His Pro Ser His Asp Leu Ile Phe Ile Phe Arg Gly Arg
340 345 350

Lys Phe Trp Ala Leu Asn Gly Tyr Asp Ile Leu Glu Gly Tyr Pro Lys
355 360 365

Lys Ile Ser Glu Leu Gly Leu Pro Lys Glu Val Lys Lys Ile Ser Ala
370 375 380

Ala Val His Phe Glu Asp Thr Gly Lys Thr Leu Leu Phe Ser Gly Asn
385 390 395 400

Gln Val Trp Arg Tyr Asp Asp Thr Asn His Ile Met Asp Lys Asp Tyr
405 410 415

Pro Arg Leu Ile Glu Glu Asp Phe Pro Gly Ile Gly Asp Lys Val Asp
420 425 430

Ala Val Tyr Glu Lys Asn Gly Tyr Ile Tyr Phe Phe Asn Gly Pro Ile
435 440 445

Gln Phe Glu Tyr Ser Ile Trp Ser Asn Arg Ile Val Arg Val Met Pro
450 455 460

Ala Asn Ser Ile Leu Trp Cys
465 470

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FIG. 1

SEQUENCE LISTING

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 <141>
 <160> 1
 15 <170> PatentIn Ver. 2.1
 <210> 1
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 20 <212> PRT
 <213> Homo sapiens
 <400> 1
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 25 1 5 10 15
 Cys Arg Ala Leu Pro Leu Pro Ser Gly Gly Asp Glu Asp Asp Leu Ser
 20 25 30
 30 Glu Glu Asp Leu Gln Phe Ala Glu Arg Tyr Leu Arg Ser Tyr Tyr His
 35 35 40 45
 Pro Thr Asn Leu Ala Gly Ile Leu Lys Glu Asn Ala Ala Ser Ser Met
 50 55 60
 35 Thr Glu Arg Leu Arg Glu Met Gln Ser Phe Phe Gly Leu Glu Val Thr
 65 70 75 80
 Gly Lys Leu Asp Asp Asn Thr Leu Asp Val Met Lys Lys Pro Arg Cys
 40 85 90 95
 Gly Val Pro Asp Val Gly Glu Tyr Asn Val Phe Pro Arg Thr Leu Lys
 100 105 110
 45 Trp Ser Lys Met Asn Leu Thr Tyr Arg Ile Val Asn Tyr Thr Pro Asp
 115 120 125
 Met Thr His Ser Glu Val Glu Lys Ala Phe Lys Lys Ala Phe Lys Val
 130 135 140
 50 Trp Ser Asp Val Thr Pro Leu Asn Phe Thr Arg Leu His Asp Gly Ile
 145 150 155 160
 Ala Asp Ile Met Ile Ser Phe Gly Ile Lys Glu His Gly Asp Phe Tyr
 165 170 175
 55 Pro Phe Asp Gly Pro Ser Gly Leu Leu Ala His Ala Phe Pro Pro Gly
 180 185 190

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FIG. 1A

	Pro	Asn	Tyr	Gly	Gly	Asp	Ala	His	Phe	Asp	Asp	Asp	Glu	Thr	Trp	Thr	
		195						200					205				
5	Ser	Ser	Ser	Lys	Gly	Tyr	Asn	Leu	Phe	Leu	Val	Ala	Ala	His	Glu	Phe	
		210					215					220					
10	Gly	His	Ser	Leu	Gly	Leu	Asp	His	Ser	Lys	Asp	Pro	Gly	Ala	Leu	Met	
	225					230					235					240	
	Phe	Pro	Ile	Tyr	Thr	Tyr	Thr	Gly	Lys	Ser	His	Phe	Met	Leu	Pro	Asp	
					245					250					255		
15	Asp	Asp	Val	Gln	Gly	Ile	Gln	Ser	Leu	Tyr	Gly	Pro	Gly	Asp	Glu	Asp	
				260					265					270			
	Pro	Asn	Pro	Lys	His	Pro	Lys	Thr	Pro	Asp	Lys	Cys	Asp	Pro	Ser	Leu	
			275					280					285				
20	Ser	Leu	Asp	Ala	Ile	Thr	Ser	Leu	Arg	Gly	Glu	Thr	Met	Ile	Phe	Lys	
		290					295					300					
25	Asp	Arg	Phe	Phe	Trp	Arg	Leu	His	Pro	Gln	Gln	Val	Asp	Ala	Glu	Leu	
	305					310					315					320	
	Phe	Leu	Thr	Lys	Ser	Phe	Trp	Pro	Glu	Leu	Pro	Asn	Arg	Ile	Asp	Ala	
					325					330					335		
30	Ala	Tyr	Glu	His	Pro	Ser	His	Asp	Leu	Ile	Phe	Ile	Phe	Arg	Gly	Arg	
				340					345					350			
	Lys	Phe	Trp	Ala	Leu	Asn	Gly	Tyr	Asp	Ile	Leu	Glu	Gly	Tyr	Pro	Lys	
			355					360					365				
35	Lys	Ile	Ser	Glu	Leu	Gly	Leu	Pro	Lys	Glu	Val	Lys	Lys	Ile	Ser	Ala	
		370					375					380					
40	Ala	Val	His	Phe	Glu	Asp	Thr	Gly	Lys	Thr	Leu	Leu	Phe	Ser	Gly	Asn	
	385					390					395					400	
	Gln	Val	Trp	Arg	Tyr	Asp	Asp	Thr	Asn	His	Ile	Met	Asp	Lys	Asp	Tyr	
					405					410					415		
45	Pro	Arg	Leu	Ile	Glu	Glu	Asp	Phe	Pro	Gly	Ile	Gly	Asp	Lys	Val	Asp	
				420					425					430			
50	Ala	Val	Tyr	Glu	Lys	Asn	Gly	Tyr	Ile	Tyr	Phe	Phe	Asn	Gly	Pro	Ile	
			435					440					445				
	Gln	Phe	Glu	Tyr	Ser	Ile	Trp	Ser	Asn	Arg	Ile	Val	Arg	Val	Met	Pro	
		450					455					460					
55	Ala	Asn	Ser	Ile	Leu	Trp	Cys										
	465					470											

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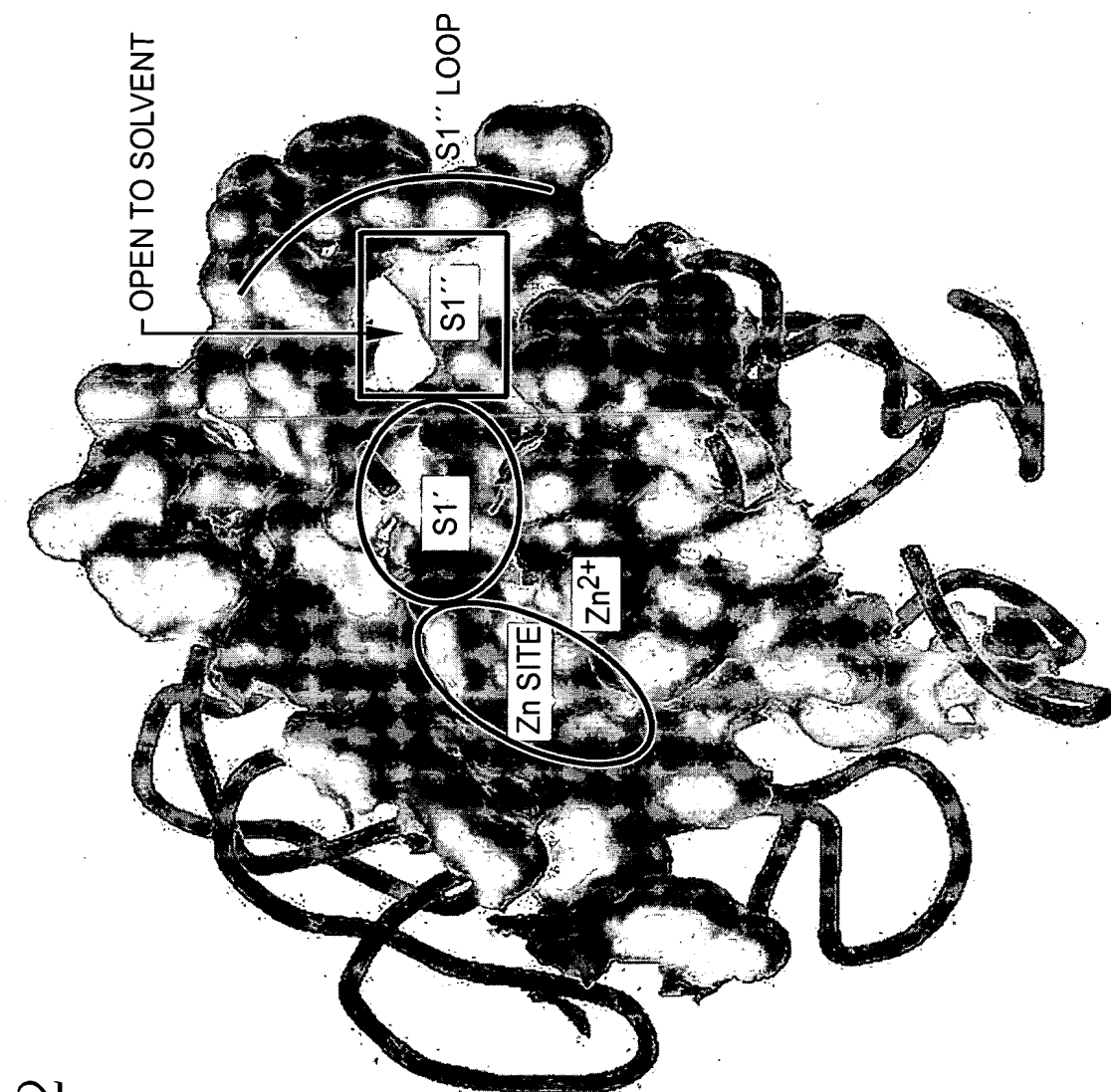


FIG. 3 SYNTHESIS EXAMPLE 1 BINDING MODE

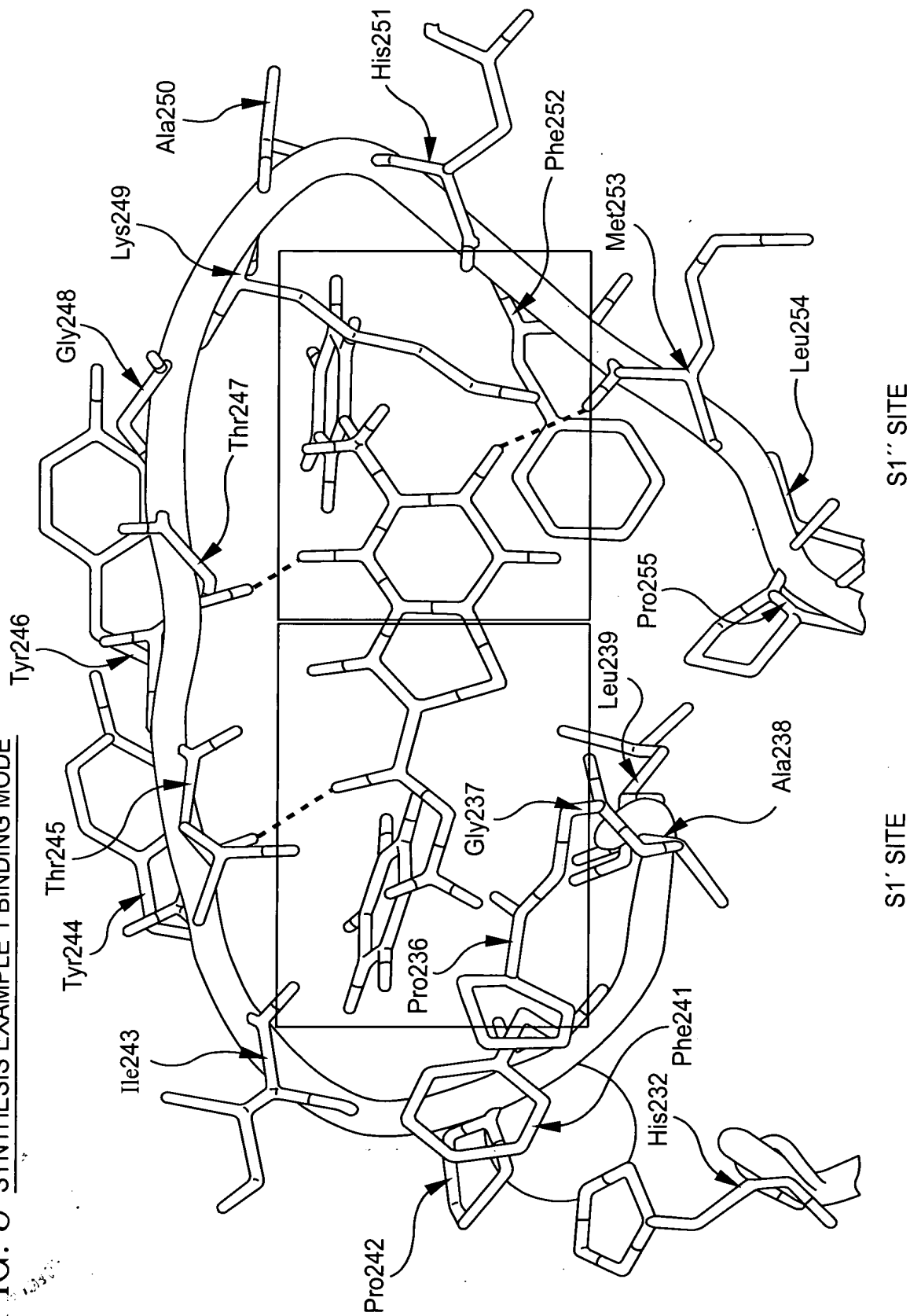
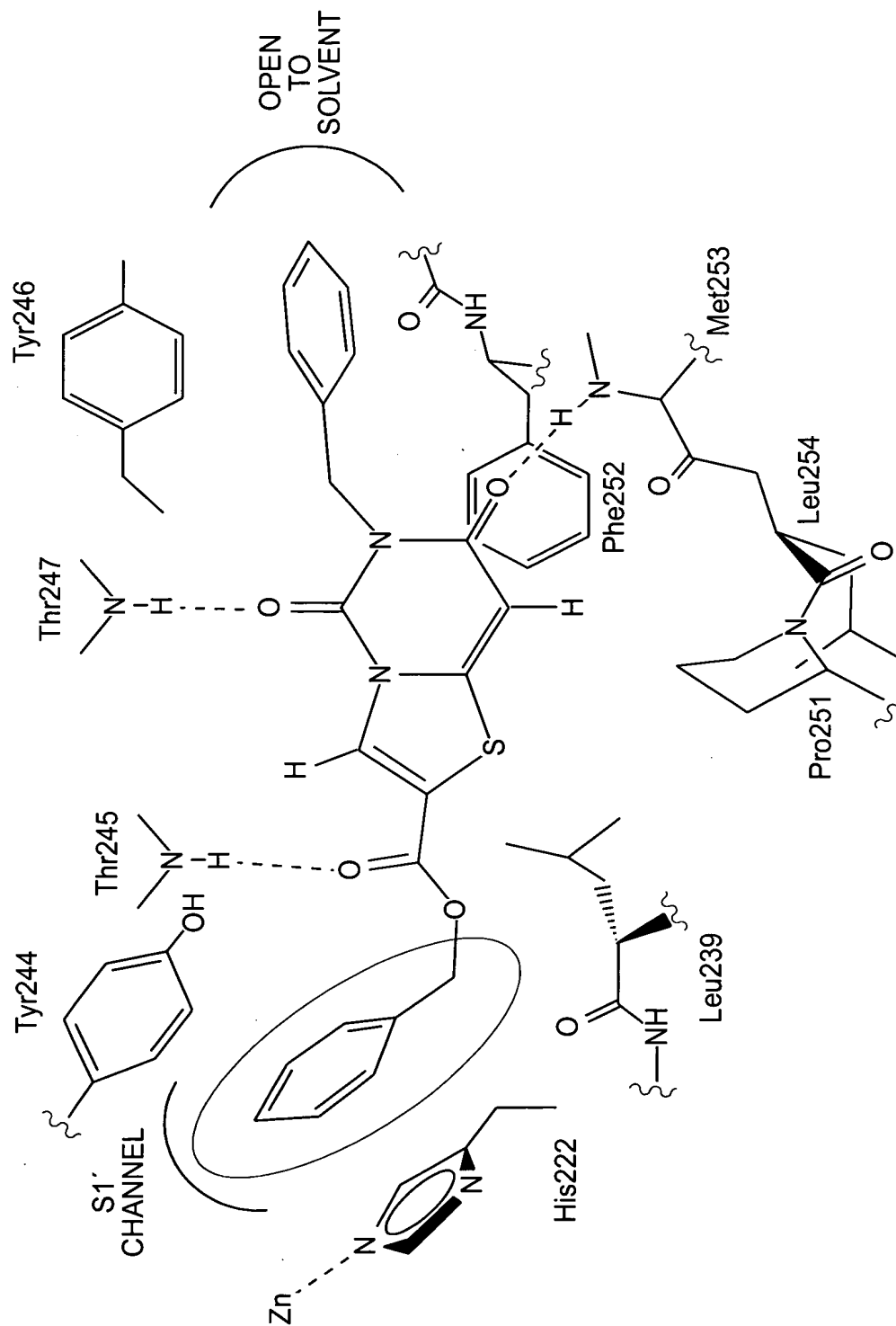
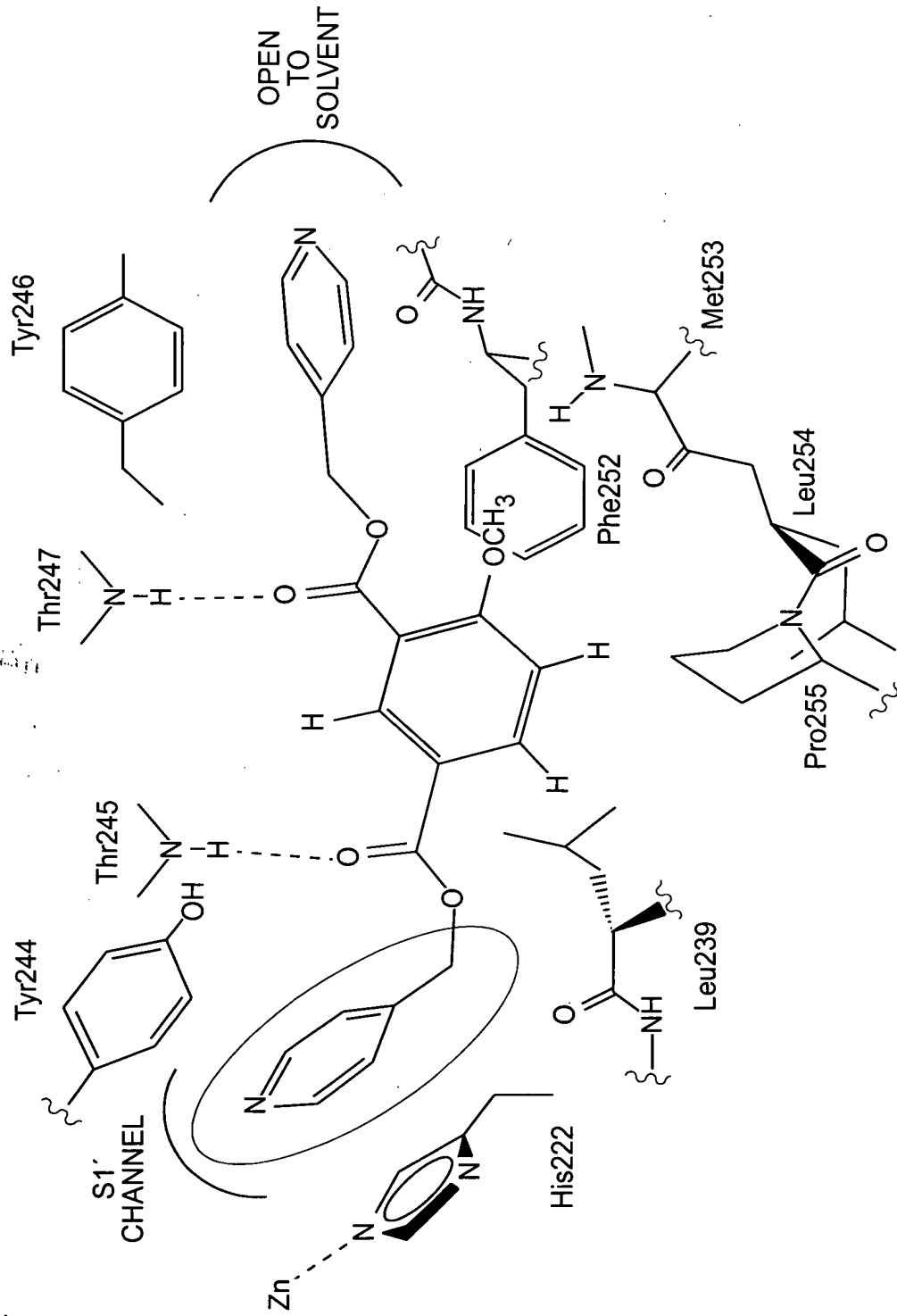


FIG. 4 SYNTHESIS EXAMPLE 1 BINDING MODE

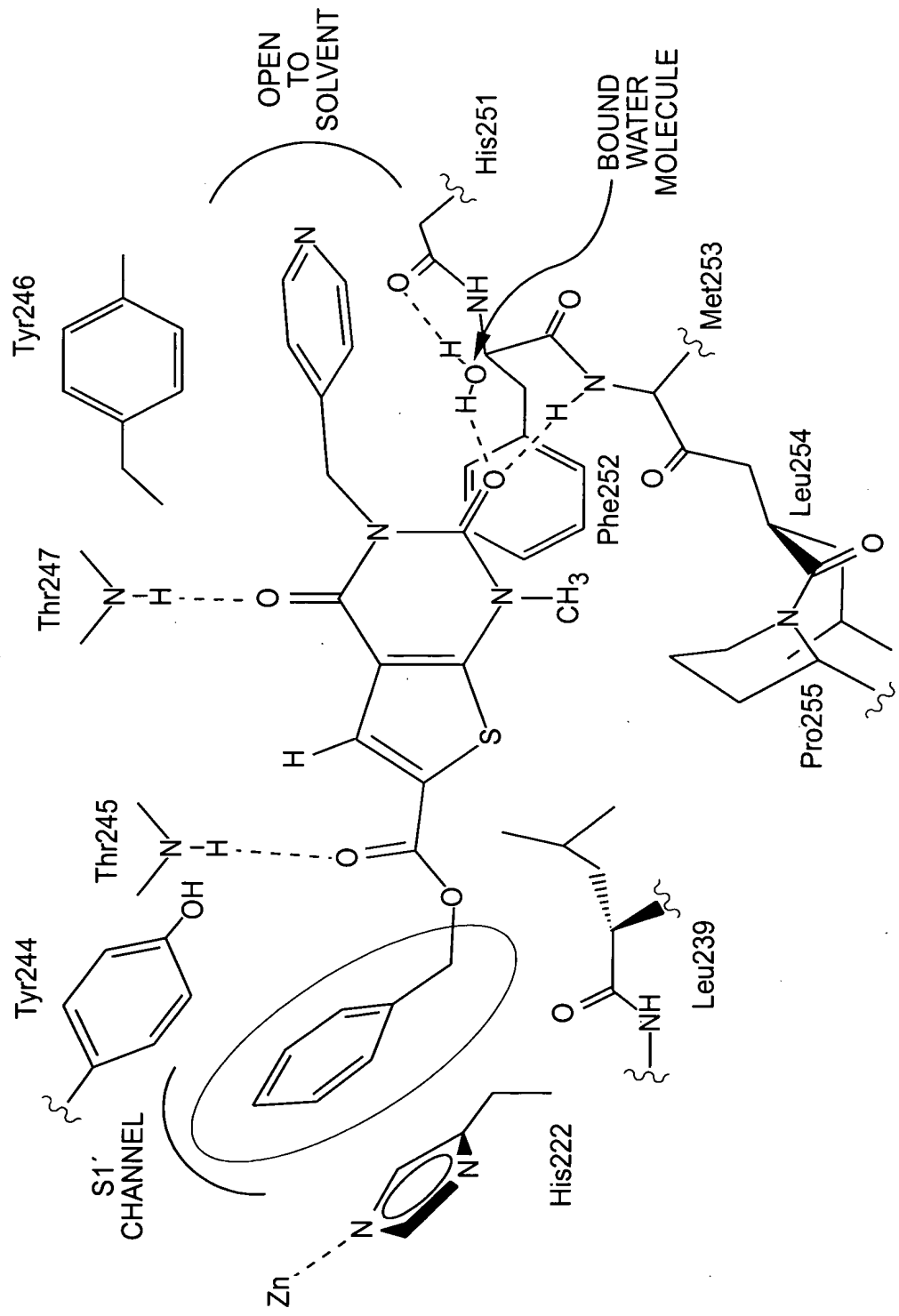


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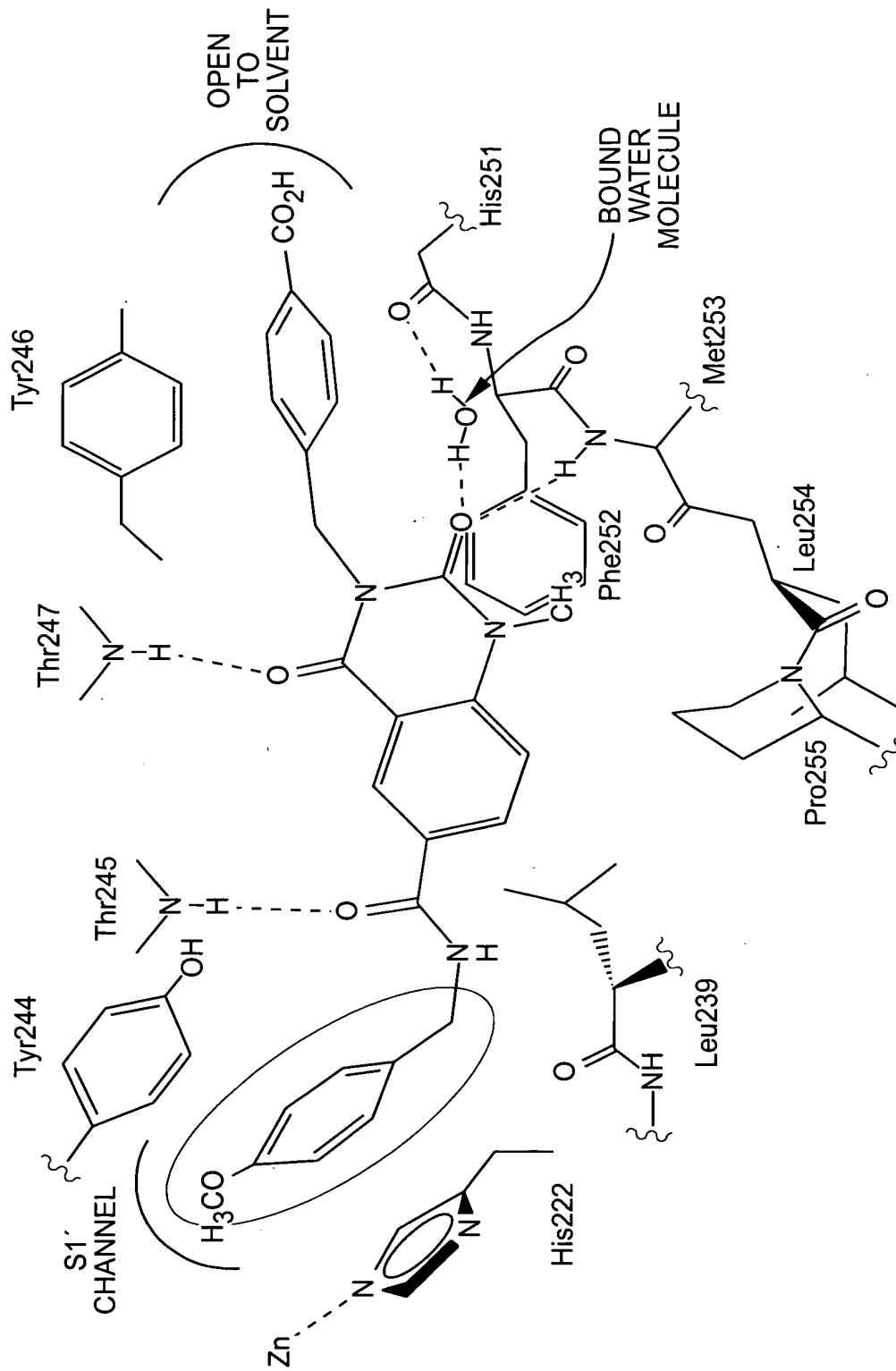
FIG. 5 SYNTHESIS EXAMPLE 10 BINDING MODE

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FIG. 6 FUSED BICYCLIC PYRIMIDONES-BINDING MODE



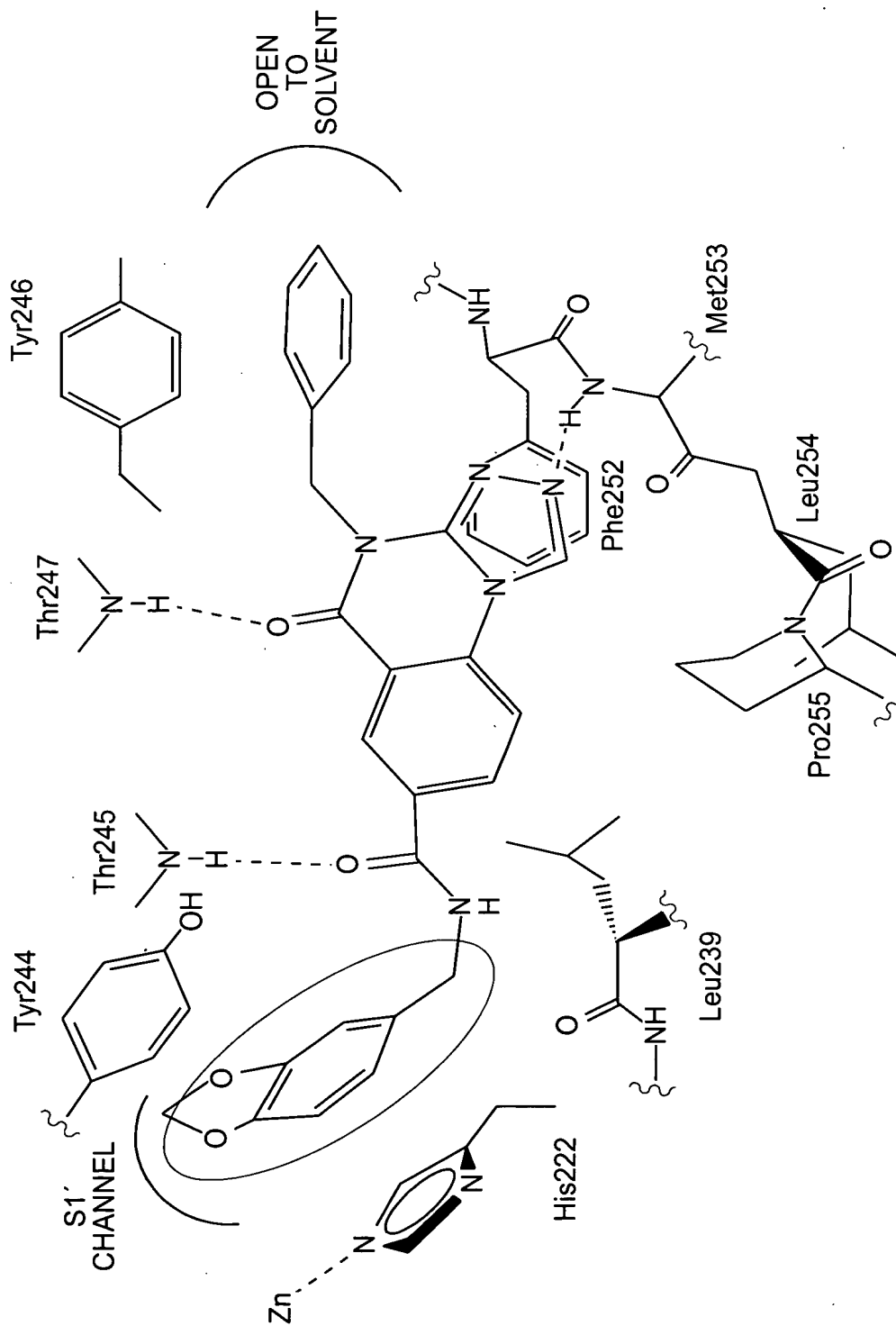
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FIG. 7 SYNTHESIS EXAMPLE 39 BINDING MODE

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FIG. 8 SYNTHESIS EXAMPLE 57 BINDING MODE



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FIG. 9. COORDONATES IN THE SPACE OF THE HYDROPHOBIC GROUPS AND HYDROGEN BOND ACCEPTORS OF THE PHARMACOPHORE

